Feasibility Study of Perfusion Imaging Using Flat Detector CT with an Intra-Arterial Injection Protocol Compared to Conventional Multi-Slice Perfusion CT with an Intravenous Injection Protocol

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Summary

This study investigated the feasibility of using intra-arterial injection-based cerebral blood volume (CBV) imaging with flat detector computed tomography (CT, IAFD-CBV). It is proven that this new method could provide comparable physiologic information as standard intravenous injection-based multi-slice computed tomography CBV imaging (IVCT-CBV).

Twelve patients were examined using both IAFD-CBV and IVCT-CBV. An experienced neuroradiologist read both sets of generated CBV maps. If a physiologic perfusion disorder was detected in standard IVCT-CBV, the focus was to check whether IAFD-CBV indicated the same disorder or not. Otherwise, if no disorder was detected, relative CBV (rCBV) values at different basal ganglia regions were measured for both CBV maps and then compared.

For three patients with lesions, IAFD-CBV and IVCT-CBV showed similar perfusion disorders in the corresponding regions. For nine patients without lesions, both CBV maps showed good symmetry of contrast agent (CA) distribution for left/right hemisphere, the total average of rCBV was found to be 0.94 –/+0.18 and 1.01 –/+0.14 (1.0 for perfect symmetry) in IAFD-CBV and IVCT-CBV, respectively. However, compared to IVCT-CBV, IAFD-CBV imaging required 70% less contrast agent (CA).

In general, a good correlation between IAFD-CBV and IVCT-CBV was found for all 12 patients. Minor deviations of IAFD-CBV were only detected at regions supplied by the middle cerebral artery. IAFD-CBV imaging, which can be directly performed in a catheterization laboratory, was proven to be technically feasible for real-time CBV assessment of the whole brain with good accuracy, and minimized CA usage.

Introduction

Nowadays, high quality soft tissue imaging can be achieved using flat detector (FD)-equipped angiographic systems, such that computed tomography (CT)-like cross-sectional images of the brain could be obtained directly within the catheterization laboratory [1-3]. This technique offers significant advantages in patient management as the patient does not have to be transferred between different clinical units, which improves clinical workflow and increases patient safety. It has been suggested that brain perfusion imaging, which displays hemodynamic information in the capillary level of the brain parenchyma, provides means to accurately evaluate the viability of the brain. Although temporal resolution of FDCT is still inadequate for dynamic perfusion imaging compared to that offered by multi-slice CT, it has

been shown that it is possible to measure the cerebral blood volume (CBV) and then display these values as a CBV map [4,5]. The CBV value generated with this technique has been validated in several animal experiments and clinical studies [6,7]. In particular, one report [8] showed that measurement of global CBV using C-arm CT in combination with either an intravenous or an ascending aorta contrast agent (CA) injection was feasible for canines with stroke.

This paper performed whole brain perfusion imaging using an FD rotational angiographic system in the catheterization laboratory for patients. To this end, an intra-arterial CA injection protocol was adopted and CBV maps were generated. For validation purposes, the resulting CBV maps were visually and quantitatively compared with those from conventional CT perfusion imaging.

Materials and Methods

Patient Selection

From December 2011 to July 2012, IAFD-CBV maps were acquired for 31 consecutive ischemic patients who were older than 18 years during diagnostic angiographic examinations. Among them, 15 patients underwent IVCT-CBV examinations within 24 hours and no interventional treatments were performed between the two examinations. Two patients were excluded from the study due to inappropriate data acquisition procedures. Another patient was also excluded because of the severe motion artifacts in the resulting images. A total of 12 patients (two female and ten male; age range, 20-76 years; mean age, 52 years) were enrolled in the study. Detailed diagnostic information on each patient is listed in Table 1. The study had been approved by the hospital ethics committee.

IAFD-CBV

A standard diagnostic cerebral angiography examination (Artis zeego, VC14, 30 cm×40 cm flat detector, Siemens Healthcare, Germany) was performed for all the patients enrolled in the study. Next, a CBV map was acquired using the same angiographic suite. A pigtail catheter was placed at the ascending aorta and 48ml of 50% diluted CA (350 mg I/ml, Iohexol 350, Beijing BEILU Pharmaceutical Co., Ltd) was injected at a rate of 3 ml/s over 16s using a power

injector (Avidia, Imaxeon, Australia). For CBV map generation, a 3D mask image was acquired first. To ensure that the brain tissue was sufficiently perfused, the second image acquisition started with an 8s X-ray delay. During image acquisition, the C-arm rotated 200 degrees in eight seconds. As an output, a total of 397 projection images were generated with an X-ray dose of 0.36 μGy/frame. The post-processing was performed using commercial software (*syngo* DynaPBV Neuro, Siemens Healthcare, Germany). The fully automatic reconstruction algorithm has been described in another paper [4].

IVCT-CBV

Within 24 hours, the patient was transferred to the radiology department for a CT perfusion examination, which was performed on a 64-section V-scanner (LightSpeed 64, GE Healthcare, USA). A monophasic injection of 80 ml CA (350 mg I/ml, Iohexol 350, Beijing BEILU Pharmaceutical Co., Ltd) was administered IV at a rate of 6ml/s and was followed by a 20 ml saline chase at the rate of 6ml/s using a power injector (Vistron, Medrad, USA). After the power injection of CA and an additional 5s prep delay, a continuous CT scan was initiated over 80 mm longitudinal range with the following parameters: 80 KVp, 200 mA, 1s per rotation for a total of 22s. Symmetry axis, venous and arterial input functions were manually selected. A semi-automatic analysis of perfusion data was performed using perfusion software (Perfusion4, GE Healthcare, USA) on a commercially available workstation (AW 4.4, GE Healthcare, USA).

Image Evaluation

An experienced neuroradiologist visually inspected both IAFD-CBV and IVCT-CBV maps of the same patient. If physiologic perfusion disorders were found in the IVCT-CBV map, the focus was on visually examining whether the IAFD-CBV map indicated the same disorder, which was shown by the illustrative case in the next section. If the patient had no physiologic perfusion disorders, a number of circular regions of interest (ROI) measuring 4 cm^2 were drawn. The ROIs were defined to cover corresponding characteristic regions for left and right hemispheres, with major vessels excluded (Figure 1). Next, spatially averaged CBV values (CBVmean) were extracted for all
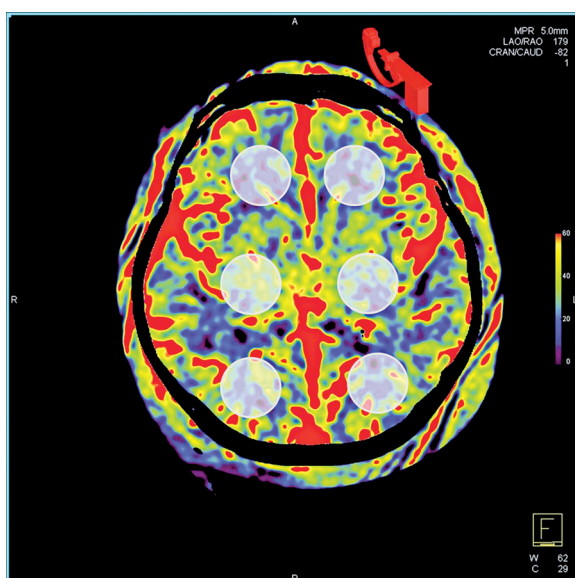
Figure 1 ROI selection covering different basal ganglia regions for left/right hemisphere in a representative CBV map.

the ROIs from both IAFD-CBV and IVCT-CBV maps. Relative CBV (rCBV) values were then calculated by:

$$rCBV = CBV_{mean\ left\ hemisphere} / CBV_{mean\ right\ hemisphere}, \quad (1)$$

and thus perfusion symmetry in basal ganglia regions supplied by the anterior, middle and posterior cerebral arteries could be quantitatively evaluated.

Results

All diagnostic information, DSA and CBV findings are summarized in Table 1. Patients #2, #5 and #6 had lesions due to lacunar infarct, intracerebral hemorrhage and Moyamoya disease, respectively. For these three patients, physiologic perfusion disorders were found in corresponding regions from both IAFD-CBV and IVCT-CBV maps through visual inspection. An illustrative case (Patient #5) is described in detail in the following section.

Illustrative Case (Patient #5)

A 40-year-old man with a long history of hypertension and hyperlipidemia had experienced hypertensive intracerebral hemorrhage at the right basal ganglia two years ago. He was treat-

Table 1 **Patients' diagnostic information**[1]

Patient No.	Clinic Diagnosis	DSA Diagnosis	CBV Finding
#1	SAH	Normal	Normal
#2	Lacunar infarction	Right-MCA occlusion	Right MCA territory infarct locus
#3	TIA	Minor stenosis at bilateral ICA and right-VA	Normal
#4	SAH	Normal	Normal
#5	Intracerebral hemorrhage	Normal	Low perfusion around right temporal lobe encephalomalacia
#6	Moyamoya disease	Bilateral ICA occlusion	Slightly increased CBV in anterior circulation
#7	TIA	Left-MCA occlusion	Normal
#8	TIA	Right-VA stenosis	Normal
#9	Cerebral infarction	Normal	Normal
#10	Intracerebral hemorrhage	Right-ICA occlusion	Normal (right-MCA territory slightly decreased)
#11	Cerebral infarction	Normal	Normal
#12	Cerebral infarction	Normal	Normal

SAH = subarachnoid haemorrhage; *TIA* = transient ischemic attack; *MCA* = middle cerebral artery; *ICA* = internal carotid artery; *VA* = vertebral artery
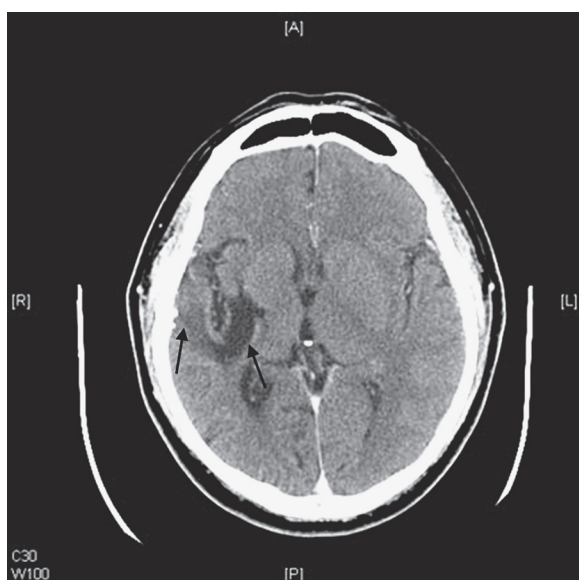
Figure 2 CT image from a representative slice. Two encephalomalacia lesions can be observed at the right basal ganglia and right temporal lobe (indicated by black arrows).
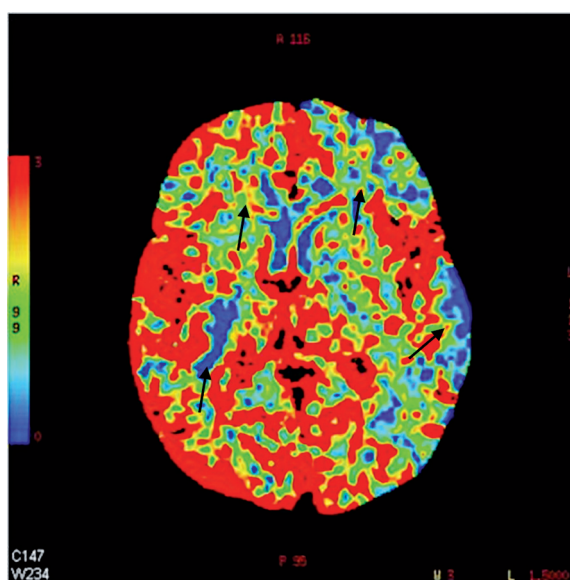

Figure 3 IVCT-CBV map from a representative slice. Black arrows indicate low perfusion regions at the right basal ganglia, left temporal lobe and bilateral frontal lobe.
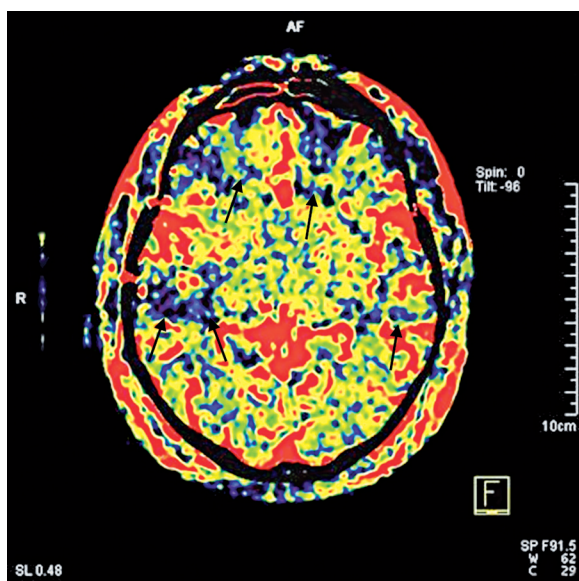

Figure 4 IAFD-CBV map from a representative slice. Black arrows indicate low perfusion regions at the right basal ganglia, bilateral frontal lobe and temporal lobe.

ed by means of brain hematoma puncture drainage and medication carried out at a local hospital. After treatment, he showed remaining symptoms of left limb weakness. The muscle strength (level 0-5, with 0 complete paralysis and 5 normal) was tested to be level 4 for the left upper limb, level 5 for left lower limb and right limbs. The muscle tension was increased in the left limb tendon, and hyperreflexia and positive pathological reflex were detected for the left limbs. CT examination showed two encephalomalacia lesions at the right basal ganglia and right temporal lobe, respectively (Figure 2).

Both IVCT-CBV and IAFD-CBV maps (Figures 3 and 4) demonstrated a similar decrease of CBV value at the right basal ganglia, which corresponded to the findings in the CT image in Figure 2. Low perfusion regions were also detected at the left temporal lobe and bilateral frontal lobes in IVCT-CBV and IAFD-CBV maps with good correlation. However,

there were no significant ischemic changes in the initial CT examinations. Besides, the patient did not show clinical symptoms which could be correlated with impairment of the corresponding regions. Thus, it was suspected that the low perfusion in these regions could be associated with peripheral arteriole sclerosis. A minor difference was mainly observed at the right temporal lobe, where a low level of perfusion was only detected on the IAFD-CBV map.

For the remaining nine patients without evident perfusion disorders (patients #1, #3, #4, #7-12), Table 2 showed the average rCBV values in the anterior, middle and posterior regions from IVCT-CBV and IAFD-CBV maps. On the IVCT-CBV map, a stable symmetry of perfusion could be found for the left/right hemisphere with rCBV values in anterior 1.00–/+0.1, middle 1.01–/+0.07, posterior 1.03–/+0.22 regions and total 1.01 –/+0.14, where all the calculated rCBV were close to 1.00. On the IAFD-CBV map, good symmetry of perfusion could be detected for anterior (0.96–/+0.15) and posterior (0.99–/+0.22) regions. Minor deviations were found in the region supplied by the MCA (0.88–/+0.08), with a rCBV value in the middle region of basal ganglia of less than 1.00. This indicated that, in general, the right hemisphere had a higher perfusion compared to the left hemisphere. The total rCBV of the IAFD-CBV map was found to be 0.94 –/+0.18.

In addition, the CA injection dose, averaged image acquisition time and post-processing time of three whole brain CBV examination approaches were compared in Table 3, where IVFD-CBV is the recommended intravenous injection protocol and typical imaging workflow for FD CT CBV (*syngo* DynaPBV Neuro, Siemens Healthcare, Germany) . It was found that IAFD-CBV required approximately one third of CA and the shortest overall time for imaging and post-processing compared to the other two approaches.

Discussion

In general, the CBV maps obtained from the IAFD-CBV matched well with the ground truth results from conventional IVCT-CBV, proving the capability of IAFD-CBV for displaying normal brain tissue and detecting lesions with good accuracy. For the three cases with abnormal low perfusion regions, the lesions at the same position on both CBV maps could be precisely detected. Moreover, this technique demonstrated higher sensitivity than IVCT-CBV for detecting a large encephalomalacia lesion, which closely corresponded to the findings in the CT image.

The remaining discrepancy, which was mainly the slight asymmetry of perfusion between left/right hemispheres in the region supplied by the MCA shown on the IAFD-CBV map, may be caused by non-uniform CA distribution. A pigtail catheter with ten side holes at the distal segment was used for CA injection. It could be observed from DSA images that for some patients, slightly larger portion of CA from the catheter tip was flowing through the ostium of the innominate artery. This may be because the ostium of innominate artery was close to the ascending aorta where the CA was injected, such that the mixture of blood and CA can easily flow directly into the innominate artery and then into the right carotid artery without changing much of flow direction. However, the ostium of the left common carotid artery was located at the aortic arch and almost perpendicu-

Table 2 **rCBV measurement in anterior, middle and posterior regions**

	In total	Anterior region	Middle region	Posterior region
IVCT-CBV	1.01 –/+ 0.14	1.00 –/+ 0.1	1.01 –/+ 0.07	1.03 –/+ 0.22
IAFD-CBV	0.94 –/+ 0.18	0.96 –/+ 0.15	0.88 –/+ 0.08	0.99 –/+ 0.22

Table 3 **Comparison of three whole brain CBV imaging approaches**

	IAFD-CBV	IVFD-CBV	IVCT-CBV
CA dose	24 ml	80 ml	80 ml
Image acquisition time	24 s	30 s	39 s
Post-processing time	29 s	29 s	191 s

lar to the flow direction, and thus, resulting in less CA flowing into the left carotid artery. In future, a new type of perfusion catheter with side holes covering the entire aortic arch (ostia of innominate artery, left common carotid artery and left subclavian artery) may result in equal CA division and help to solve the asymmetric perfusion issue.

The key clinical benefit of IAFD-CBV is that it enables repeated real time monitoring of brain function and assessments of perfusion parameters during an interventional procedure in the angiographic suit, which is clinically essential for treating certain neurovascular diseases such as stroke management [9-10]. For instance, during ischemic cerebrovascular disease intervention, IAFD-CBV imaging can be performed before and after treatment, reflecting functional changes of the brain and enabling a direct evaluation on the treatment outcome.

Another advantage of IAFD-CBV is the significant reduction of CA dose for acquiring perfusion information on the whole brain. The conventional intravenous injection protocols typically require 80 ml CA to be injected, where only a very small portion contributes to the creation of CBV images. Compared to the intra venous approach, intra-arterial injection is much more efficient requiring only 24 ml CA injected, which potentially reduces CA-induced side-effects.

In addition, using IAFD-CBV, it is also pos-sible to achieve functional analysis of parts of the brain by selectively injecting CA into one artery (vertebral or carotid arteries). In this way, clinicians can focus solely on examining CBV changes in the lesion region without being distracted by irrelevant regions.

The limitations of our study should be also mentioned. Firstly, user intervention was required to manually select the arterial input function and symmetry axis for generating IVCT-CBV maps. It has been discussed that the discrepancy caused by manual operation may impact on the image formation process and CBV measurement [11,12]. Secondly, the number of patients recruited in this study was limited, which preliminarily demonstrated that CBV maps obtained using FDCT were comparable with those from conventional perfusion CT.

Conclusion

This study tested and confirmed the feasibility of using FDCT with intra-arterial CA injection within the angiographic suite to acquire CBV maps. This technique offered the possibility to obtain functional information on the whole brain during the interventional procedure. Future work should be extended to include a larger number of patients with more clinical scenarios and to eliminate non-uniform CA distribution.

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